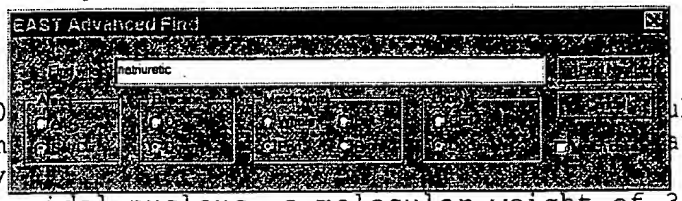
today in an effort to prevent or reverse these pathologic states. However, most potent widely used diuretics not only increase sodium excretion but may also lead to undesirable loss of potassium. Unfortunately, the potassium supplements prescribed for replacement are generally unpalatable, expensive and difficult for patients to tolerate on a continuing basis.

(8) There thus exists a need for a potent natriuretic compound which specifically augments sodium excretion but does not produce the loss of potassium. The present invention satisfies this need and provides related advantages as well.



(9)

(10) ubstantially purified natriuretic com at increases sodium excretion without adv The Natriuretic Hormone has a steroidal nucleus, a molecular weight of 360.4 and a molecular formula of C.sub.21 H.sub.28 O.sub.5.

(11) In one aspect of the invention, the Natriuretic Hormone is obtained by lyophilizing and reconstituting at a reduced volume with deionized water the urine from uremic patients to obtain concentrated samples, separating the concentrated material by gel filtration, subjecting the post salt peak to reverse-phase high pressure liquid chromatography using a pyridinium acetate/methanol buffer. The biologically active material activity is eluted with about 45% methanol. The purified product of the HPLC is then trimethylsilylated and subjected to gas chromatography at elevated temperature. The single product of this chromatography is then hydrolyzed in acid solutions to yield after evaporation the Natriuretic Hormone.

(12) In another aspect of the invention, the Natriuretic Hormone is used to increase the sodium excretion in a mammal.

specific activity. Specific binding of[.sup.125 l]-human ANP (ANP) and [.sup.125 l]-porcine BNP (pBNP) to transfected cells was determined in the presence or absence of unlabeled peptides. Cells expressing either the NPRB or NPRA receptors specifically bound three fold more [.sup.125 l]-ANP each, and 3- to 4-fold more [.sup.125 l]-pBNP, respectively, than control cells (Table 2). Note that the specific activity of [.sup.125 l]-pBNP is 3-fold less than [.sup.125 l]-ANP (Table 2).

Detailed Description Text - DETX (47):

Ligand-dependent activation of the cytoplasmic GC domains of the human NPRB and NPRA receptors was examined in transient expression whole-cell stimulation assays. Cells expressing the NPRA responded alike to stimulation by either ANP or pBNP, with a 1.5 to 2-fold increase in cGMP produced over control transfected cells (FIG. 3, A and C). Cells expressing the NPRB responded to ANP stimulation with a 3-fold increase in cGMP synthesized as compared to control transfected cells. Quite strikingly, pBNP gave a 9.7 fold increase in cGMP for the NPRB over pBNP treated control transfected cells (FIG. 3, B and C). The pBNP ligand is 6.4-fold more effective that ANP in the activation of NPRB GC activity. Human B natriuretic peptide (hBNP) is compared with ANP in the whole cell stimulation assays. We note that there is only 70% identity between human and porcine BNP as opposed to the high sequence conservation of ANP's between species.sup.18. Although comparison of the predicted amino acid sequence from a partial porcine NPRB cDNA to the human NPRB reveals 99% identity for 736 residues, the response of these receptors to their homologous BNP ligands is different. Nevertheless, the use of pBNP and ANP allows pharmacological discrimination of human NPRA and NPRB via the magnitude of GC activation.

Detailed Description Text - DETX (90):

Polyclonal antibodies to NPRB generally are raised in animals by multiple subcutaneous (sc) or interperitoneal (ip) injections of NPRB and an adjuvant

Detailed Description Text - DETX (90):
Polyclonal antibodies to NPRB generally are raised in animals by multiple subcutaneous (sc) or interperitoneal (ip) injections of NPRB and an adjuvant. It may be useful to conjugate NPRB or a fragment containing the target amino acid sequence to a protein which is immunogenic in the species to be immunized, e.g., keyhole limpet hemocyanin, serum albumin, bovine thryoglobulin, or soybean trypsin inhibitor using a bifunctional or derivatizing agent, for example, maleimidobenzoyl sulfosuccinimide ester (conjugation through cystein residues), N-hydroxysuccinimide (through lysine residues), glutaraldehyde, succinic anhydride, SOCl.sub.2, or R.sup.1 N.dbd.C.dbd.NR.

Detailed Description Text - DETX (95):
Suitably diagnostic assays for NPRB and its antibodies are well known per se. In addition to the bioassay described above, competitive, sandwich and steric inhibition immunoassay techniques are useful. The competitive and sandwich methods employ a phase separation step as an integral part of the method while steric inhibition assays are conducted in a single reaction mixture. Fundamentally, the same procedures are used for the assay of NPRB and for substances that bind NPRB, although certain methods will be favored depending upon the molecular weight of the substance being assayed. Therefore, the substance to be tested is referred to herein as an analyte, irrespective of its status otherwise as an antigen or antibody, and proteins which bind to the analyte are denominated binding partners, whether they be antibodies, cell surface receptors or antigens.

Detailed Description Text - DETX (97):
The label used is any detectable functionality which does not interfere with the binding of analyte and its binding partner. Numerous labels are known for use in immunoassay, examples including enzymes such as horseradish peroxidase

Suitably diagnostic assays for NPRB and its antibodies are well known per se. In addition to the bioassay described above, competitive, sandwich and steric inhibition immunoassay techniques are useful. The competitive and sandwich methods employ a phase separation step as an integral part of the method while steric inhibition assays are conducted in a single reaction mixture. Fundamentally, the same procedures are used for the assay of NPRB and for substances that bind NPRB, although certain methods will be favored depending upon the molecular weight of the substance being assayed. Therefore, the substance to be tested is referred to herein as an analyte, irrespective of its status otherwise as an antigen or antibody, and proteins which bind to the analyte are denominated binding partners, whether they be antibodies, cell surface receptors or antigens.

Detailed Description Text - DETX (97):

The label used is any detectable functionality which does not interfere with the binding of analyte and its binding partner. Numerous labels are known for use in immunoassay, examples including enzymes such as horseradish peroxidase, radioisotopes such as .sup.14 C and .sup.131 I, fluorophores such as rare earth chelates or fluorescein, stable free radicals and the like. Conventional methods are available to covalently bind these labels to proteins or polypeptides. Such bonding methods are suitable for use with NPRB or its antibodies, all of which are proteinaceous.

Detailed Description Text - DETX (106):

The NPRB may be used as a binding ligand in affinity purification of those molecules having specific affinity for the NPRB, such as ANP, BNP and CNP. Methods of immuno purifying both known and unknown ligands are described in Current Protocols in Molecular Biology, volume 2, John Wiley & Sons, New York, 1989, chapter 10, particularly pages 10.11.1 to 10.17.1.